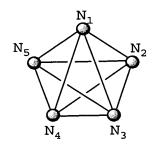
## Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

## **Listing of Claims:**

Claim 1 (Currently Amended) A compound comprising the atom corresponding to  $N_3$  and the two or more atoms selected from  $N_1$ ,  $N_2$ ,  $N_4$  and  $N_5$ , said atoms constitute the pharmacophore represented by the following formula 1:



wherein N<sub>1</sub> represents an atom to which a donative hydrogen atom in a hydrogen-bond donating group is bonded or a hydrogen-bond accepting atom in a hydrogen-bond accepting group; N<sub>3</sub> represents a hydrogen-bond accepting atom in a hydrogen-bond accepting group; and N<sub>2</sub>, N<sub>4</sub> and N<sub>5</sub> independently represent an arbitrary carbon atom constituting a hydrophobic group and the distance between N<sub>1</sub> and N<sub>2</sub> is not less than 5 angstroms and not more than 12 angstroms, the distance between N<sub>1</sub> and N<sub>3</sub> is not less than 9 angstroms and not more than 15 angstroms, the distance between N<sub>1</sub> and N<sub>4</sub> is not less than 3 angstroms and not more than 13 angstroms, the distance between N<sub>1</sub> and N<sub>5</sub> is not less than 8 angstroms and not more than 16 angstroms, the distance between N<sub>2</sub> and N<sub>3</sub> is not less than 6 angstroms and not more than 10 angstroms, the distance between N<sub>2</sub> and N<sub>4</sub> is not less than 9 angstroms and not more than 14 angstroms, the distance between N<sub>2</sub> and N<sub>5</sub> is not less than 9 angstroms and not more than 14 angstroms, the distance between N<sub>3</sub> and N<sub>4</sub> is not less than 4 angstroms and not more than 11 angstroms, the distance between N<sub>3</sub> and N<sub>4</sub> is not less than 3 angstroms and not more than 11 angstroms, the distance between N<sub>3</sub> and N<sub>4</sub> is not less than 3 angstroms and not

more than 10 angstroms, and the distance between  $N_4$  and  $N_5$  is not less than 4 angstroms and not more than 9 angstroms; and, in the optimized three-dimensional structure thereof, the distances between the atom corresponding to  $N_3$  and the two or more atoms selected from  $N_1$ ,  $N_2$ ,  $N_4$  and  $N_5$  are the interatomic distances in the pharmacophore; and a salt thereof, with the proviso that the compound can not be a benzene derivative of the formula:

## wherein:

R<sup>1</sup> and R<sup>2</sup> each is hydrogen or lower alkyl;

R<sup>3</sup> is hydrogen, phenyl, substituted phenyl or lower alkyl;

R<sup>4</sup> to R<sup>8</sup> each being hydrogen, halogen, lower alkyl, lower alkoxy, cyano, trifluoromethyl, hydroxyl, lower acyl, lower alkoxycarbonyl, N,N-diloweralkylaminocarbonyl, or N,N-loweralkyleneaminocarbonyl with at least two of R<sup>4</sup> to R<sup>8</sup> being hydrogen and each of R<sup>5</sup> to R<sup>7</sup> each optionally being carboxy; and

 $R^9$  to  $R^{11}$  each being hydrogen, halogen, cyano, lower alkyl, lower alkoxy, carboxy or nitro with at least one of  $R^9$  to  $R^{11}$  being hydrogen.

Claim 2 (Original) A compound or a salt thereof according to Claim 1, wherein, for each of the atoms constituting the pharmacophore, the distance between  $N_1$  and  $N_2$  is not less than 5.09 angstroms and not more than 11.67 angstroms, the distance between  $N_1$  and  $N_3$  is not less than 9.47 angstroms and not more than 14.30 angstroms, the distance between  $N_1$  and

 $N_4$  is not less than 3.48 angstroms and not more than 12.60 angstroms, the distance between  $N_1$  and  $N_5$  is not less than 8.77 angstroms and not more than 15.67 angstroms, the distance between  $N_2$  and  $N_3$  is not less than 3.78 angstroms and not more than 9.78 angstroms, the distance between  $N_2$  and  $N_4$  is not less than 6.97 angstroms and not more than 13.26 angstroms, the distance between  $N_2$  and  $N_5$  is not less than 9.37 angstroms and not more than 13.32 angstroms, the distance between  $N_3$  and  $N_4$  is not less than 4.83 angstroms and not more than 10.51 angstroms, the distance between  $N_3$  and  $N_5$  is not less than 3.31 angstroms and not more than 9.97 angstroms, and the distance between  $N_4$  and  $N_5$  is not less than 4.32 angstroms and not more than 8.25 angstroms.

Claim 3 (Previously Presented) A compound or a salt thereof according to Claim 1, wherein N<sub>1</sub> constituting the pharmacophore is a nitrogen atom of unsubstituted or substituted amino, ammonium, amido, thioamido, ureido, isoureido, amidino, guanidino, thioureido, hydrazino or hydrazono group to which one or more hydrogen atoms are bonded, a carbon atom of ethenyl group to which a hydrogen atom is bonded, an oxygen atom of carbonyl group, a sulfur atom of thiocarbonyl group, a nitrogen atom of unsubstituted or substituted imino group, an oxygen atom of sulfonyl group, an oxygen atom of sulfonyloxy group, an oxygen atom of sulfo group, an oxygen atom of thioether, a sulfur atom of mercapto group, an oxygen atom of hydroxyl group, an oxygen atom of ester or a nitrogen atom of unsubstituted or substituted nitrogen-containing heterocyclic group; N<sub>3</sub> is an oxygen atom of carbonyl group, a sulfur atom of thiocarbonyl group, a nitrogen atom of unsubstituted or substituted imino group, an oxygen atom of sulfo group, an oxygen atom of sulfonyl group, an oxygen atom of ether, a sulfur atom of thioether, an oxygen atom of carboxyl group, an oxygen atom of ether, a sulfur atom of thioether, an oxygen atom of

hydroxyl group, an oxygen atom of ester, a nitrogen atom of unsubstituted or substituted nitrogen-containing heterocyclic group to which no hydrogen atom is combined, a nitrogen atom of sulfonamido group or a nitrogen atom of acylsulfonamido group; and each of  $N_2$ ,  $N_4$  and  $N_5$  is an arbitrary carbon atom constituting a carbon atom of alkyl group, a carbon atom of alkenyl group, a carbon atom of aryl group and a carbon atom of alkoxy group.

Claim 4 (Previously Presented) A compound or a salt thereof according to Claim 1, wherein a compound having an atom corresponding to  $N_3$  and atoms corresponding to two or more atoms selected from  $N_1$ ,  $N_2$ ,  $N_4$  and  $N_5$  among the atoms  $N_1$ ,  $N_2$ ,  $N_3$ ,  $N_4$  and  $N_5$  constituting a pharmacophore, and, in the optimized three-dimensional structure thereof, the interatomic distances between the atom corresponding to  $N_3$  and the two or more atoms selected from  $N_1$ ,  $N_2$ ,  $N_4$  and  $N_5$  are the atomic distances of a pharmacophore has an activity of antagonistically inhibiting the binding between AP-1 (activator protein-1) and a recognition sequence thereof.

Claim 5 (Withdrawn) A peptide of 10 residues represented by the following amino acid sequence:

wherein Ac represents an acetyl group, AA<sup>3</sup> represents a polar amino acid residue, each of AA<sup>4</sup>, AA<sup>6</sup> and AA<sup>7</sup> represents a hydrophobic amino acid residue, AA<sup>5</sup> represents an amino acid residue having carboxyl or hydroxyl group in the side chain thereof, and AA<sup>8</sup> represents an arbitrary amino acid residue; said peptide having a disulfide linkage between the first and tenth cysteine residues; or a salt thereof.

Claim 6 (Withdrawn) A peptide or a salt thereof according to Claim 5, wherein AA<sup>3</sup> is an L-asparagine residue or an L-glutamine residue; AA<sup>4</sup>, AA<sup>6</sup> and AA<sup>7</sup> are an L-leucine residue, an L-isoleucine residue, an L-alanine residue or an L-valine residue; and AA<sup>5</sup> is an L-aspartic acid residue, an L-glutamic acid residue, an L-serine residue or an L-threonine residue.

Claim 7 (Withdrawn) A peptide of 10 or 11 residues represented by the following amino acid sequence:

wherein Ac represents an acetyl group, aa<sup>0</sup> represents an arbitrary amino acid residue or a bonding unit, aa<sup>3</sup> represents a polar amino acid residue, each of aa<sup>4</sup>, aa<sup>5</sup> and aa<sup>7</sup> represents a hydrophobic amino acid residue, aa<sup>6</sup> represents an arbitrary amino acid residue, and aa<sup>9</sup> represents an amino acid residue having carboxyl or hydroxyl group in the side chain thereof; provided that, when aa<sup>0</sup> is a bonding unit, said peptide has a disulfide linkage between the first and tenth cysteine residues and, when aa<sup>0</sup> is an arbitrary amino acid residue, said peptide has a disulfide linkage between the second and eleventh cysteine residues; or a salt thereof.

Claim 8 (Withdrawn) A peptide or a salt thereof according to Claim 7, wherein aa<sup>3</sup> is an L-asparagine acid residue or an L-glutamine acid residue; aa<sup>4</sup>, aa<sup>5</sup> and aa<sup>7</sup> are an L-leucine residue, an L-isoleucine residue, an L-alanine residue or an L-valine residue; and aa<sup>9</sup> is an L-aspartic acid residue, an L-glutamic acid residue, an L-serine residue or an L-threonine residue.

Claim 9 (Currently Amended) A benzene derivative represented by the following general formula:

$$R^1$$
 $X^1$ 
 $R^3$ 
 $R^4$ 

wherein R<sup>1</sup> represents a halogen atom, a cyano group, a nitro group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group: R<sup>3</sup> represents a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group, a carbamoyl group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; R<sup>4</sup> represents a hydrogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group;

X<sup>1</sup> represents -C(O)-, -CH(OH)-, -CH<sub>2</sub>- or a group of the following formula:

7

Application No. 09/830,559
Reply to the Office Action dated March 25, 2004

$$R^{21}-O$$
 $R^{22}$ 
 $R^{23}$ 
 $R^{24}$ 
 $R^{25}$ 
 $R^{25}$ 

wherein R<sup>21</sup> represents an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl or heterocycle-lower alkyl group; R<sup>22</sup> and R<sup>23</sup> may be the same or different represent a hydrogen atom or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl, carbamoyl, alkylsulfinyl, alkylsulfonyl, arylsulfonyl or heterocyclic group; and R<sup>24</sup> and R<sup>25</sup> may be the same or different represent a hydrogen atom, a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; the double line of which one line is a broken line denotes a single bond or a double bond; and

W represents -Z-COR<sup>26</sup>, -Z-COOR<sup>2</sup>, -O-CH<sub>2</sub>COOR<sup>2</sup> or -O-CH<sub>2</sub>CH<sub>2</sub>COOR<sup>2</sup> [wherein Z represents -(CH<sub>2</sub>)<sub>n</sub>- in which n represents 0, 1, 2 or 3, -CH<sub>2</sub>CH(CH<sub>3</sub>)-, -CH=CH- or -CH<sub>2</sub>CH=CH-; R<sup>2</sup> represents a hydrogen atom or a protecting group for carboxyl group; and R<sup>26</sup> represents -NHR<sup>27</sup> or -NHSO<sub>2</sub>R<sup>28</sup> in which R<sup>27</sup> and R<sup>28</sup> independently represent an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl or aralkyl group];

or a salt thereof.

Claim 10 (Currently Amended) A benzene derivative or a salt thereof according to Claim 9, wherein W is -Z'-COOR<sup>2'</sup>, -Z'-CONH-SO<sub>2</sub>R<sup>28'</sup>, -CONH-CH<sub>2</sub>COOR<sup>2'</sup> or -CONH-CH<sub>2</sub>COOR<sup>2'</sup> wherein Z' represents -(CH<sub>2</sub>)<sub>n'</sub>- in which n' is 0, 1 or 2, or -CH=CH-; R<sup>28'</sup>

represents an unsubstituted or substituted alkyl group; and  $R^{2'}$  represents a hydrogen atom or a protecting group for carboxyl group; and  $X^{1}$  is -C(O)-, -CH(OH)- or -CH<sub>2</sub>-.

Claim 11 (Withdrawn) A benzene derivative or a salt thereof according to Claim 10, wherein R<sup>1</sup> is an unprotected or protected hydroxyl group or an unsubstituted or substituted alkoxy group; R<sup>3</sup> is an unprotected or protected hydroxyl group or an unsubstituted or substituted alkoxy group; and R<sup>4</sup> is an unprotected or protected hydroxyl group or an unsubstituted or substituted or substituted alkoxy group.

Claim 12 (Withdrawn) A benzene derivative represented by the following general formula:

$$R^5$$
 $R^5$ 
 $R^5$ 
 $R^5$ 
 $R^5$ 
 $R^5$ 
 $R^5$ 

wherein R<sup>5</sup> represents a hydrogen atom, a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; R<sup>6</sup> represents a hydrogen atom or a protecting group for carboxyl group; X<sup>2</sup> represents -C(O)-; m represents 0, 1 or 2; and ring A represents a group represented by the following formula:

wherein R7 represents a hydrogen atom, a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; and R8 represents a hydrogen atom, an unprotected or protected amino group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; or a group of the following formula:

wherein R<sup>9</sup> and R<sup>10</sup> may be the same or different represent a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino, alkanoyloxy or heterocyclic group;

Claim 13 (Withdrawn) A benzene derivative or a salt thereof according to Claim 12, wherein  $R^5$  is an alkoxy group or an acylamino group;  $X^2$  is -C(O)-; and ring A is a group of the following formula:

wherein  $R^{11}$  is an alkyl or alkoxycarbonyl group; and  $R^{12}$  is an alkyl group; or a group of the following formula:

wherein R<sup>13</sup> is an alkyl or alkoxycarbonyl group; and R<sup>14</sup> is an alkoxy or alkanoyloxy group.

Claim 14 (Withdrawn) A benzene derivative represented by the following general formula:

wherein R<sup>15</sup> and R<sup>16</sup> may be the same or different represent a hydrogen atom, a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl,

Application No. 09/830,559
Reply to the Office Action dated March 25, 2004

alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group;  $X^3$  represents -C(O)-; and ring B represents a group of the following formula:

wherein R<sup>17</sup> represents a hydrogen atom or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylsulfonyl or heterocyclic group; R<sup>18</sup> represents a hydrogen atom or a protecting group for carboxyl group; and p represents 0, 1 or 2;

or a salt thereof.

Claim 15 (Withdrawn) A benzene derivative or a salt thereof according to Claim 14, wherein R<sup>15</sup> and R<sup>16</sup> may be the same or different represent an alkoxy group; and ring B represents a group of the following formula:

wherein  $R^{19}$  is an acyl group;  $R^{20}$  is a protecting group for carboxyl group; and p is 0, 1 or 2.

Claim 16 (Previously Presented) A benzene derivative represented by the following formula:

$$R^{1a}$$
 $W^{a}$ 
 $X^{1a}$ 
 $R^{3a}$ 
 $R^{4a}$ 

wherein R<sup>1a</sup> represents a halogen atom, a cyano group, a nitro group, an unprotected or protected hydroxyl group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; R<sup>3a</sup> and R<sup>4a</sup> may be the same or different represent a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; X<sup>1a</sup> represents -C(O)-, -CH(OH)-, -CH<sub>2</sub>- or a group of the following formula:

$$R^{21a}-O$$
 $R^{22a}$ 
 $R^{23a}$ 
 $R^{24a}$ 
 $R^{25a}$ 

wherein R<sup>21a</sup> represents an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl or heterocycle-lower alkyl group; R<sup>22a</sup> and R<sup>23a</sup> may be the same or different represent a hydrogen atom or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl, carbamoyl, alkylsulfinyl, alkylsulfonyl, arylsulfonyl or heterocyclic group; R<sup>24a</sup> and R<sup>25a</sup> may be the same or different represent a hydrogen atom, a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylsulfinyl, alkylsulfonyl,

alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; and the double line of which one line is a broken line represents a single bond or a double bond; and  $W^a$  represents  $-Z^a$ - $COR^{26a}$ ,  $-Z^a$ - $COOR^{2a}$ , -O- $CH_2COOR^{2a}$  or -O- $CH_2CH_2COOR^{2a}$  [wherein  $Z^a$  represents  $-(CH_2)_n^a$  ( $n^a$  is 0, 1, 2 or 3),  $-CH_2CH(CH_3)$ -, -CH=CH- or  $-CH_2CH$ =CH-;  $R^{2a}$  represents a hydrogen atom or a protecting group for carboxyl group; and  $R^{26a}$  represents  $-NHR^{27a}$  or  $-NHSO_2R^{28a}$  in which  $R^{27a}$  and  $R^{28a}$  independently represent an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl or aralkyl group];

or a salt thereof.

Claim 17 (Currently Amended) A benzene derivative or a salt thereof according to Claim 16, wherein R<sup>1a</sup> is an unprotected or protected hydroxyl group or an unsubstituted or substituted alkoxy group; R<sup>3a</sup> and R<sup>4a</sup> may be the same or different and represent an unprotected or protected hydroxyl group or an unsubstituted or substituted alkoxy group; X<sup>1a</sup> is -C(O)-, -CH(OH)-, -CH<sub>2</sub>- or a group of the following formula:

wherein R<sup>21a'</sup> represents an unsubstituted or substituted alkyl, aralkyl or heterocycle-lower alkyl group; R<sup>24a'</sup> and R<sup>25a'</sup> may be the same or different represent a hydrogen atom, an unprotected or protected carboxyl group or an unsubstituted or substituted alkyl, alkoxycarbonyl, aryloxycarbonyl or carbamoyl group; and W<sup>a</sup> represents -Z<sup>a'</sup>-COR<sup>26a'</sup>, -Z<sup>a'</sup>-COOR<sup>2a'</sup>, -O-CH<sub>2</sub>COOR<sup>2a'</sup>, -O-CH<sub>2</sub>COOR<sup>2a'</sup>, -CONH-CH<sub>2</sub>COOR<sup>2a'</sup>, or -CONH-CH<sub>2</sub>COOR<sup>2a'</sup> wherein Z<sup>a'</sup> represents -(CH<sub>2</sub>)<sub>n</sub><sup>a'</sup>- in which n<sup>a'</sup> is 0, 1, 2 or 3, -CH<sub>2</sub>CH(CH<sub>3</sub>)-, -CH=CH- or -CH<sub>2</sub>CH=CH-; R<sup>2a'</sup> represents a hydrogen atom or a protecting

group for carboxyl group; and  $R^{26a'}$  represents -NHSO<sub>2</sub> $R^{28a'}$  in which  $R^{28a'}$  is an unsubstituted or substituted alkyl group.

Claim 18 (Currently Amended) A benzene derivative represented by the following general formula:

$$R^{1b}$$
 $Z^{b}$ 
 $Z^{b}$ 
 $R^{4b}$ 

wherein R<sup>1b</sup> represents a halogen atom, a cyano group, a nitro group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonyl, alkylsulfonylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; R<sup>2b</sup> represents a hydrogen atom or a protecting group for carboxyl group; R<sup>3b</sup> and R<sup>4b</sup> may be the same or different represent a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; X<sup>1b</sup> represents -C(O)-, -CH(OH)- or -CH<sub>2</sub>-; and Z<sup>b</sup> represents -(CH<sub>2</sub>)<sub>n</sub><sup>b</sup>- (n<sup>b</sup> represents 0, 1 or 2) or -CH=CH-;

Claim 19 (Original): A benzene derivative or a salt thereof according to Claim 18, wherein  $R^{1b}$  is an unsubstituted or substituted alkoxy group;  $R^{3b}$  and  $R^{4b}$  may be the same or different represent an unprotected or protected hydroxyl group or an unsubstituted or substituted alkoxy group;  $X^{1b}$  is -C(O)-; and  $Z^{b}$  is -(CH<sub>2</sub>)<sub>2</sub>-.

Claim 20 (Currently Amended) A benzene derivative represented by the following general formula:

$$R^{1c}$$
 $Z^{c}$ 
 $R^{4c}$ 
 $R^{4c}$ 

wherein R<sup>1c</sup> represents a halogen atom, a cyano group, a nitro group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; R<sup>2c</sup> represents a hydrogen atom or a protecting group for carboxyl group; R<sup>3c</sup> and R<sup>4c</sup> may be the same or different represent a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; X<sup>1c</sup> represents -C(O)-, -CH(OH)- or -CH<sub>2</sub>-; and Z<sup>c</sup> represents -(CH<sub>2</sub>)<sub>n</sub><sup>c</sup> - (n<sup>c</sup> represents 0, 1 or 2) or -CH=CH-;

Claim 21 (Original) A benzene derivative or a salt thereof according to Claim 20, wherein  $R^{1c}$  is an unsubstituted or substituted alkoxy group;  $R^{2c}$  is a hydrogen atom or a protecting group for carboxyl group;  $R^{3c}$  and  $R^{4c}$  may be the same or different represent an unsubstituted or substituted alkoxy group;  $X^{1c}$  represents -C(O)-; and  $Z^{c}$  represents -(CH<sub>2</sub>)<sub>2</sub>-.

Claim 22 (Withdrawn) A benzene derivative represented by the following general formula:

wherein R<sup>1d</sup> represents a halogen atom, a cyano group, a nitro group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; R<sup>2d</sup> represents a hydrogen atom or a protecting group for carboxyl group; R<sup>3d</sup> represents a hydrogen atom or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl or aralkyl group; R<sup>4d</sup> represents a halogen atom, a nitro group, an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl, alkoxycarbonyl, aryloxycarbonyl, alkylsulfonyl, alkylsulfonylamino or arylsulfonylamino group; X<sup>1d</sup> represents -C(O)-, -CH(OH)- or -CH<sub>2</sub>-; and Z<sup>d</sup> represents -(CH<sub>2</sub>)nd - (nd represents 0, 1 or 2) or -CH=CH-;

Claim 23 (Withdrawn) A benzene derivative or a salt thereof according to Claim 22, wherein  $R^{1d}$  is an unsubstituted or substituted alkoxy group;  $R^{3d}$  is an unsubstituted or substituted alkyl group;  $R^{4d}$  is an unsubstituted or substituted acyl group;  $X^{1d}$  is -C(O)-; and  $Z^d$  is -(CH<sub>2</sub>)<sub>2</sub>-.

Claim 24 (Withdrawn) A benzene derivative represented by the following general formula:

$$R^{2e}$$
OOC  $Z^{e}$ 
 $R^{1e}$ 
 $R^{1e}$ 
 $R^{4e}$ 

wherein R<sup>0e</sup> represents a hydrogen atom, a halogen atom, a nitro group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl, alkoxycarbonyl, aryloxycarbonyl, alkylsulfonylamino or arylsulfonylamino group; R<sup>1e</sup> represents an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl, alkoxycarbonyl, aryloxycarbonyl or alkylsulfonyl group; R<sup>2e</sup> represents a hydrogen atom or a protecting group for carboxyl group; R3e and R4e may be the same or different represent a hydrogen atom, a halogen atom, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, alkylthio, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; X1e represents -C(O)-, -CH(OH)- or -CH2-; and Ze represents -(CH2)ne-(ne represents 0, 1 or 2) or -CH=CH-;

Claim 25 (Withdrawn) A benzene derivative or a salt thereof according to Claim 24, wherein  $R^{0e}$  is a hydrogen atom or a halogen atom;  $R^{1e}$  is an unsubstituted or substituted alkyl group;  $R^{3e}$  and  $R^{4e}$  independently represent an unsubstituted or substituted alkoxy group;  $X^{1e}$  is -C(O)-; and  $Z^{e}$  is a bonding unit.

Claim 26 (Withdrawn) A benzene derivative represented by the following general formula:

$$\mathbb{R}^{1f} \xrightarrow{\mathbb{Z}^{f}} \mathbb{Coor}^{2f} \mathbb{R}^{4f}$$

wherein R<sup>1f</sup> represents a halogen atom, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, alkylthio, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; R2f represents a hydrogen atom or a protecting group for carboxyl group; R3f and R4f may be the same or different represent a hydrogen atom or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl or aralkyl group; X1f represents -C(O)-, -CH(OH)- or -CH2-; and Zf represents -(CH2)nf- (nf represents 1 or 2) or -CH=CH-;

or a salt thereof.

Claim 27 (Withdrawn) A benzene derivative or a salt thereof according to Claim 26, wherein  $R^{1f}$  is an unsubstituted or substituted alkoxy group;  $R^{3f}$  and  $R^{4f}$  independently represent an unsubstituted or substituted alkyl group;  $X^{1f}$  is -C(O)-; and  $Z^f$  is -CH<sub>2</sub>-.

Claim 28. (Currently Amended) A benzene derivative represented by the following general formula:

$$R^{1g}$$
 $Z^{g}$ 
 $Z^{g}$ 
 $Z^{g}$ 
 $Z^{g}$ 

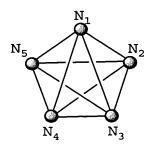
wherein  $R^{1g}$  and  $R^{4g}$  may be the same or different represent an unprotected or protected hydroxyl group or an unsubstituted or substituted alkoxy group;  $X^{1g}$  is -C(O)-, -CH(OH)- or -CH<sub>2</sub>-;  $Z^g$  is -(CH<sub>2</sub>)<sub>n</sub><sup>g</sup>- (n<sup>g</sup> represents 1 or 2); and  $R^{2g}$  is a hydrogen atom or a protecting group for carboxyl group;

or a salt thereof.

Claim 29 (Previously Presented) A compound or a salt thereof according to Claim 9, wherein said compound is a compound that has an activity of antagonistically inhibiting the combination between AP-1 and a recognition sequence thereof.

Claim 30 (Previously Presented) A compound comprising the atom corresponding to  $N_3$  and the two or more atoms selected from  $N_1$ ,  $N_2$ ,  $N_4$  and  $N_5$ , said atoms constitute the pharmacophore represented by the following formula 1:

20



wherein N<sub>1</sub> represents an atom to which a donative hydrogen atom in a hydrogen-bond donating group is bonded or a hydrogen-bond accepting atom in a hydrogen-bond accepting group; N<sub>3</sub> represents a hydrogen-bond accepting atom in a hydrogen-bond accepting group; and N2, N4 and N5 independently represent an arbitrary carbon atom constituting a hydrophobic group and the distance between N<sub>1</sub> and N<sub>2</sub> is not less than 5 angstroms and not more than 12 angstroms, the distance between N<sub>1</sub> and N<sub>3</sub> is not less than 9 angstroms and not more than 15 angstroms, the distance between N1 and N4 is not less than 3 angstroms and not more than 13 angstroms, the distance between N<sub>1</sub> and N<sub>5</sub> is not less than 8 angstroms and not more than 16 angstroms, the distance between N2 and N3 is not less than 3 angstroms and not more than 10 angstroms, the distance between N2 and N4 is not less than 6 angstroms and not more than 14 angstroms, the distance between N<sub>2</sub> and N<sub>5</sub> is not less than 9 angstroms and not more than 14 angstroms, the distance between N<sub>3</sub> and N<sub>4</sub> is not less than 4 angstroms and not more than 11 angstroms, the distance between N<sub>3</sub> and N<sub>5</sub> is not less than 3 angstroms and not more than 10 angstroms, and the distance between N<sub>4</sub> and N<sub>5</sub> is not less than 4 angstroms and not more than 9 angstroms; and, in the optimized three-dimensional structure thereof, the distances between the atom corresponding to N<sub>3</sub> and the two or more atoms selected from N<sub>1</sub>,  $N_2$ ,  $N_4$  and  $N_5$  are the interatomic distances in the pharmacophore; and a salt thereof, wherein the compound conforming to a pharmacophore is a peptide or benzene derivative according to Claim 9.

Claim 31 (Withdrawn) A method for inhibiting AP-1 which comprises administering a compound or a salt thereof according to Claim 1.

Claim 32 (Previously Presented) An agent for preventing and treating a disease into which an excessive expression of AP-1 participates, which comprises a compound or a salt thereof according to Claim 1.

Claim 33 (Previously Presented) An agent for preventing and treating an autoimmune disease, which comprises a compound or a salt thereof according to Claim 1.

Claim 34 (Previously Presented) An AP-1 inhibitor comprising a compound or a salt thereof according to Claim 1.

Claim 35 (Previously Presented) A compound or a salt thereof according to Claim 9, wherein said compound is a compound that has an activity of antagonistically inhibiting the combination between AP-1 and a recognition sequence thereof.

Claim 36 (Canceled).

Claim 37 (Previously Presented) A method for inhibiting AP-1 which comprises administering a compound or a salt thereof according to Claim 9.

Claim 38 (Previously Presented) An agent for preventing and treating a disease into which an excessive expression of AP-1 participates, which comprises a compound or a salt thereof according to Claim 9.

Claim 39 (Previously Presented) An agent for preventing and treating an autoimmune disease, which comprises a compound or a salt thereof according to Claim 9.

Claim 40 (Previously Presented) An AP-1 inhibitor comprising a compound or a salt thereof according to Claim 9.

Claim 41 (Previously Presented) A benzene derivative according to Claim 9, having the following formula:

Claim 42 (Previously Presented) A benzene derivative according to Claim 12, having the following formula:

23

Application No. 09/830,559 Reply to the Office Action dated March 25, 2004

Claim 43 (Previously Presented) The benzene derivative according to Claim 14, having the following formula:

Claim 44 (Previously Presented) A benzene derivative according to Claim 16, having the formula:

Application No. 09/830,559 Reply to the Office Action dated March 25, 2004

Claim 45 (Previously Presented) A benzene derivative according to Claim 18, having the formula:

Claim 46 (Previously Presented) The benzene derivative according to Claim 20, having the formula:

Application No. 09/830,559
•Reply to the Office Action dated March 25, 2004

Claim 47 (Previously Presented) The benzene derivative according to Claim 22, having the formula:

Claim 48 (Previously Presented) The benzene derivative according to Claim 24, having the formula:

Application No. 09/830,559
Reply to the Office Action dated March 25, 2004

Claim 49 (Previously Presented) The benzene derivative according to Claim 26, having the formula:

Claim 50 (Previously Presented) The benzene derivative according to Claim 28, having the formula:

Claim 51 (New) A benzene derivative represented by the following formula:

wherein R<sup>1b</sup> represents a halogen atom, a cyano group, a nitro group, a protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; R<sup>2b</sup> represents a hydrogen atom or a protecting group for carboxyl group; R<sup>3b</sup> and R<sup>4b</sup> may be the same or different represent a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; X<sup>1b</sup> represents -C(O)-, -CH(OH)- or -CH<sub>2</sub>-; and Z<sup>b</sup> represents -(CH<sub>2</sub>)<sub>n</sub><sup>b</sup>- (n<sup>b</sup> represents 0, 1 or 2) or -CH=CH-;

or a salt thereof.

Claim 52 (New) A benzene derivative represented by the following formula:

$$R^{1c}$$
 $Z^{c}$ 
 $R^{4c}$ 
 $R^{4c}$ 

wherein R<sup>1c</sup> represents a halogen atom, a cyano group, a nitro group, a protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; R<sup>2c</sup> represents a hydrogen atom

Application No. 09/830,559
Reply to the Office Action dated March 25, 2004

or a protecting group for carboxyl group;  $R^{3c}$  and  $R^{4c}$  may be the same or different represent a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group;  $X^{1c}$  represents -C(O)-, -CH(OH)- or -CH<sub>2</sub>-; and  $Z^{c}$  represents -(CH<sub>2</sub>) $_{n}^{c}$  - ( $n^{c}$  represents 0, 1 or 2) or -CH=CH-;

or a salt thereof.

Claim 53. (New) A benzene derivative represented by the following formula:

$$R^{1g}$$
 $Z^{g}$ 
 $COOR^{2g}$ 

wherein  $R^{1g}$  is a protected hydroxyl group and  $R^{4g}$  an unprotected or protected hydroxyl group or an unsubstituted or substituted alkoxy group;  $X^{1g}$  is -C(O)-, -CH(OH)- or -CH<sub>2</sub>-;  $Z^g$  is -(CH<sub>2</sub>)<sub>n</sub><sup>g</sup>- (n<sup>g</sup> represents 1 or 2); and  $R^{2g}$  is a hydrogen atom or a protecting group for carboxyl group;